Eur J Vasc Endovasc Surg **18**, 122–126 (1999)
Article No. ejvs.1999.0852

Diabetes Mellitus as a Risk Factor for Early Outcome After Carotid Endarterectomy – a Population-based Study

Abdi Ahari[1], on behalf of the Swedish Vascular Registry (Swedvasc)*
Steering committee: David Bergqvist[1]†, Thomas Troëng[2], Johan Elfström[3], Bengt Hedberg[4], K.-G. Ljungström[5], Lars Norgren[6] and Per Örtenwall[7]

Departments of Surgery: [1]Uppsala University Hospital, [2]Karlskrona County Hospital, [3]Linköping University Hospital, [4]Halmstad County Hospital, [5]Danderyd Hospital, [6]Lund University Hospital and [7]Göteborg University Hospital, Sweden

Background and purpose: *to determine if diabetes mellitus is a risk factor for outcome after carotid endarterectomy (CEA).*
Methods: *the outcome and complications of all vascular procedures performed in Sweden are registered prospectively in the Swedish Vascular Registry (Swedvasc) and form the basis of this report. During the 10-year period 1987–96 2622 CEAs were analysed for notified complications.*
Results: *of the 2622 CEAs, 341 (13%) were performed on diabetics and 2281 (87%) on non-diabetics. Patients with diabetes presented at a younger age (67.1 ± 8.3 years vs. 68.2 ± 8.3 years; p = 0.028), were more likely to have a history of hypertension (61.9% vs. 50%; p = 0.001) and were less often smokers (34.9% vs. 43.2%; p = 0.001). Diabetics presented more often with minor stroke (41.3% vs. 30.8%; p = 0.002) and non-diabetics more often with amaurosis fugax (18.9% vs. 14.4%; p = 0.04). Diabetics had a higher 30-day mortality (3.2% vs. 1.4%; p = 0.02). The 30-day neurologic and cardiac morbidity did not differ. The 1-year mortality was 7.9% in diabetics and 4.4% in non-diabetics (p = 0.008). Non-diabetics operated on in 1992–96 compared to those operated on in 1987–91 had a significantly lower combined permanent stroke and death rate (3.7% vs. 5.7%; p = 0.05), a difference not found in diabetics (6.3% for 1987–92 and 6.8% for 1992–96; N.S.).*
Conclusions: *diabetics had both a higher 30-day and 1-year mortality after CEA compared to non-diabetics, mainly because of cardiac complications. However, postoperative neurologic morbidity did not differ.*

Key Words: Diabetes mellitus; Carotid endarterectomy; Stroke.

Introduction

Diabetes mellitus is a major risk factor for the development of ischaemic stroke. Patients with diabetes are at least two times more likely to suffer from a stroke than non-diabetics.[1,2] The difference persists even when adjusted for hypertension, cholesterol, smoking, obesity, and, after excluding individuals with previous history of stroke, myocardial infarction (MI) or congestive heart failure (CHF).[3] In addition, stroke in diabetics is associated with worse functional outcome and higher mortality compared to non-diabetics.[4–6]

The benefit of carotid endarterectomy (CEA), in selected patients with symptomatic high-grade internal carotid artery (ICA) stenosis, is confirmed in several randomised clinical trials.[7–9] However, the long-term benefit of CEA is dependent on low perioperative stroke and mortality rates. The major causes of serious perioperative morbidity and mortality are stroke and cardiovascular disease.[10,11]

Some investigators have suggested that diabetics have a higher incidence of postoperative complications after CEA.[12,13] On the other hand, others have not found a significant difference in stroke and death between the two groups.[14,15] We have analysed data on a population basis from the Swedish Vascular Registry. The aim of this study was to compare diabetics and non-diabetics regarding clinical presentation, the 30-day postoperative neurologic and cardiac morbidity, and the 30-day and 1-year mortality in order to define the safety of CEA in the diabetic population.

* See acknowledgements for full list of participating centres and surgeons.
† Please address all correspondence to: D. Bergqvist, Department of Surgery, Uppsala University Hospital, S-751 85 Uppsala, Sweden.

1078–5884/99/080122 + 05 $12.00/0

Table 1. Preoperative risk factors registered in Swedvasc.

	Preoperative risk factors
1	History of stroke or TIA
2	Diabetes (controlled diet, oral hypoglycaemic medication or insulin-dependent)
3	Hypercholesterolaemia (>2SD from normal value)
4	Hypertension (medicated or untreated diastolic pressure >110 mmHg)
5	History of MI, angina pectoris, pathologic ECG, arrhythmia, CHF, CABG
6	Previous vascular surgery, angioplasty, amputation due to vascular disease
7	Chronic lung disease
8	S-creatinine >150 μmol/l
9	Smoker or former smoker during the last five years

TIA: transient ischaemic attack; MI: myocardial infarction; CHF: congestive heart failure; CABG: coronary artery bypass graft.

Materials and Methods

The Vascular Registry in Sweden (Swedvasc) started as a regional registry, in the southern parts of the country, with a population base of 1.9 million. It has gradually expanded, now covering more than 8.5 million people (basically the total Swedish population).[16,17] The participating centres report all open vascular and endovascular surgical procedures. Reoperations and complications are reported. Results are reported on standardised forms after 30 days and 1 year. Mortality data can be cross-checked with The National Population Registry, making survival analysis possible after the 1-year clinical follow-up. All centres performing carotid artery surgery in Sweden participate in the registry and report their results. Validation against anaesthesia registries and reproducibility control of random samples of cases are performed regularly confirming a more than 90% report rate and 90% reproducibility of data.[18]

From January 1987 to December 1996 a total of 2708 carotid endarterectomies, performed on 2501 patients, were registered in Swedvasc; of these procedures, 341 were performed on patients registered as diabetics (controlled diet, oral hypoglycaemic medication or insulin-dependent: it is not possible to distinguish the three treatment modalities), 2033 registered as non-diabetics, 13 registered as diabetes unknown and in 321 cases missing values with no registration for diabetes. Due to the large number of missing values, these were analysed separately.

Diabetes is one of several risk factors reported to Swedvasc (Table 1). Of the 321 procedures with missing values for diabetes, 248 had one or more risk factors other than diabetes registered. Of these 248 patients a sample of 120 patient records were analysed for risk factors, showing that when a risk factor was left as a missing value it was negative in 94.8% and positive in 5.2% of the cases. It therefore seems safe to assume that a missing value in these patients can be considered as a negative value. On the other hand, when all risk factors are left as missing values, which was the case in 73 operations, it is more likely that it is due to inadequate notification of risk factors. Together with the 13 operations where diabetes was registered as unknown, these 73 operations were excluded from our analysis. This resulted in a total of 341 (13%) CEAs performed on 313 diabetics and 2281 (87%) procedures on 2102 non-diabetics analysed in our report.

The clinical presentation leading to CEA was classified in the following five groups: asymptomatic, amaurosis fugax (transient monocular visual loss), TIA (ischaemic hemispheric symptoms lasting <24 h), minor stroke (non-disabling stroke) and other causes. The 30-day postoperative neurologic morbidity was classified as: TIA/AF when there was full recovery within 24 h, transient stroke when the neurologic deficit lasted more than 24 h but less than 30 days, and permanent stroke when the neurologic deficit lasted more than 30 days. In 46 patients, postoperative neurologic morbidity was only registered as a postoperative neurologic event, with no further specification. Records for these 46 patients were analysed and classified as TIA/AF, transient or permanent stroke. All neurologic events are reported regardless of whether ipsilateral or contralateral to the CEA. All deaths within 30 days of the operation are reported, regardless of cause. All cardiac events within 30 days are reported.

Data management and statistical analysis were performed using the SPSS for Windows program package. Categorical variables were compared with Fisher's exact test and continuous variables with Student's t-test. Preoperative variables that were positively associated with postoperative outcome at a p value less than 0.1 were selected for multivariate analysis using binary logistic regression analysis. All tests were two-tailed, and a level of significance set at $p \leq 0.05$.

Results

Demographic data are reported in Table 2. Patients with diabetes presented at a younger age (67.1 ± 8.3 years) compared with non-diabetics (68.2 ± 8.3 years; $p = 0.028$). A significantly greater percentage of non-diabetics were smokers (43.2% vs. 34.9%; $p = 0.001$). Diabetics had a significantly higher rate of hypertension (61.9%) compared to non-diabetics (50%; $p = 0.001$). There was no difference in the frequency of previous heart disease between diabetic and non-diabetic patients (48.7% vs. 44.1%; N.S.). Previous vascular

Table 2. Clinical characteristics.

	Diabetic patients $n = 341$ (13%)	Non-diabetic patients $n = 2281$ (87%)	p
Age (year; mean ± S.D.)	67.1 ± 8.3	68.2 ± 8.3	0.028
Sex			
Male	215 (63%)	1537 (67.4%)	N.S.
Female	126 (37%)	744 (32.6%)	
Smoking			
Smoker	119 (34.9%)	985 (43.2%)	0.001
Non-smoker	222 (65.1%)	1296 (56.8%)	
History of hypertension			
Hypertension	211 (61.9%)	1140 (50.0%)	0.001
No hypertension	130 (38.1%)	1141 (50.0%)	
History of heart disease			
Heart disease	166 (48.7%)	1007 (44.1%)	N.S.
No heart disease	175 (51.3%)	1274 (55.9%)	
Previous vascular surgery			
Previous surgery	66 (19.4%)	442 (19.4%)	N.S.
No previous surgery	275 (80.6%)	1839 (80.6%)	
History of pulmonary disease			
Pulmonary disease	21 (6.2%)	130 (5.7%)	N.S.
No pulmonary disease	320 (93.8%)	2151 (94.3%)	
History of renal disease			
Renal disease	14 (4.1%)	81 (3.6%)	N.S.
No renal disease	327 (95.9%)	2200 (96.4%)	

Table 3. Clinical presentation.

	Diabetic patients $n = 341$ (13%)	Non-diabetic patients $n = 2281$ (87%)	p
Asymptomatic	30 (8.8%)	216 (9.5%)	N.S.
Amaurosis fugax	49 (14.4%)	431 (18.9%)	0.04
TIA	109 (32.0%)	837 (36.7%)	N.S.
Minor stroke	141 (41.3%)	702 (30.8%)	0.002
Other	12 (3.5%)	95 (4.2%)	N.S.

surgery had been performed in 19.4% of both groups. Diabetics presented significantly more often with minor stroke (41.3%) compared to non-diabetics (30.8%; $p = 0.002$), and non-diabetics presented more often with amaurosis fugax (18.9% vs. 14.4%; $p = 0.04$). Other clinical presentations did not differ (Table 3).

The 30-day permanent stroke rate was 3.5% in the diabetics and 2.8% in the non-diabetics (N.S.). Transient stroke developed in 1.5% of the diabetics and 2.4% of the non-diabetics (N.S.), and TIA/AF in 1.8% of the diabetics and 1.9% of the non-diabetics (N.S.). Diabetics had a significantly higher 30-day mortality (3.2%) compared with non-diabetics (1.4%; $p = 0.02$). Apart from diabetes, a history of previous heart disease was an independent risk factor for the 30-day mortality (Table 4). The major 30-day cause of death was cardiovascular disease (45.5% diabetics, 45.2% non-diabetics) followed by cerebrovascular disease (36.4% diabetics, 38.7% non-diabetics) with no significant difference between the two groups. By univariate analysis the combined 30-day permanent stroke and death rate was significantly higher among diabetics (6.7%) compared with non-diabetics (4.1%; $p = 0.035$). By logistic regression analysis, however, hypertension was the only independent risk factor for combined 30-day permanent stroke and mortality ($p = 0.02$). The total 30-day postoperative cardiac morbidity (MI, angina, CHF, arrhythmia) was 4.7% in diabetics and 3.7% in non-diabetics (N.S.). The 1-year mortality after CEA was significantly higher among diabetics (7.9% vs. 4.4%; $p = 0.008$). Previous heart disease and the male gender proved also to be independent risk factors for 1-year mortality by logistic regression analysis (Table 4).

Non-diabetics operated on in 1992–96 compared to those operated on in 1987–91 had a significantly lower combined 30-day permanent stroke and death rate (3.7% vs. 5.7%; $p = 0.05$). This decrease in the morbidity and mortality was not found in diabetic patients, who had a combined permanent stroke and death rate of 6.3% for 1987–92 and 6.8% for 1992–96 (N.S.).

Discussion

Continuous audit of morbidity and mortality after CEA is of great importance for identifying risk factors and reducing complications. Reviews of data coming from single institutions are of limited value, since they represent the experience of the surgeon(s) preparing the report.[19] Population-based audits provide better insight in the average risk of perioperative complications.[20] An important finding in our series was the significantly increased 30-day and 1-year mortality in diabetic patients. However, diabetic patients did not show an increase in postoperative neurologic events, neither transient nor permanent. There are several possible explanations for the higher mortality in diabetics after CEA. Diabetics more frequently underwent surgery for minor stroke, which in turn has a higher postoperative complication rate than asymptomatic stenosis or TIA/AF. The incidence of preoperative hypertension was also higher.

Being a multicentre registry study, there are several limitations that should be taken into consideration when interpreting our results. Our study is totally dependent on surgeons all around the country reporting their results and complications accurately. The registry, which is designed for all vascular procedures

Table 4. Multivariate analysis.

	30-day combined stroke and mortality		30-day mortality		1-year mortality	
	Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate
Gender	$p=0.69$	$p=0.71$	$p=0.18$	$p=0.17$	$p=0.012$	$p=0.02$
Smoking	$p=0.34$	$p=0.50$	$p=0.87$	$p=0.95$	$p=0.65$	$p=0.35$
Diabetes	$p=0.035$	$p=0.07$	$p=0.014$	$p=0.02$	$p=0.009$	$p=0.008$
Hypertension	$p=0.006$	$p=0.02$	$p=0.054$	$p=0.09$	$p=0.056$	$p=0.12$
Heart disease	$p=0.046$	$p=0.10$	$p=0.01$	$p=0.047$	$p=0.001$	$p=0.001$
Previous vascular procedure	$p=0.28$	$p=0.48$	$p=0.1$	$p=0.24$	$p=0.065$	$p=0.28$

The combined end-point stroke and mortality at 30 days was chosen because it is usually in publications on CEA. Otherwise, mortality was the main end-point.

and not specifically for CEAs, has some shortcomings. The degree of internal carotid stenosis is not reported, neither is the presence of contralateral pathology nor the use of peroperative shunting. Information about method of anaesthesia is not registered. Cardiac morbidity is not described in detail. Various cardiac events (MI, angina, CHF, arrhythmia) are all reported as postoperative cardiac morbidity. One problem is how reliable the registry is in reporting stroke, but there seem to be few missed ones.[21] Finally, with patients coming from many centres, having been operated on by different surgeons and with partially different routines as for pre- and postoperative care, unrecognised confounding variables may have been included in our review.

There are few previous studies directly focusing on CEA in diabetic patients and how outcome is influenced by the diabetic disease. Akbari *et al.*[14] neither found a difference in postoperative neurologic morbidity (2.1% diabetics vs. 1.1% non-diabetics; $p=0.28$) nor mortality (0.3% total mortality) between diabetics and non-diabetics. Their patients were followed up for complications during their postoperative hospital stay (4.1 ± 0.4 days in diabetics and 3.2 ± 0.2 days in non-diabetics) and not for a full 30-day period, although previous trials[7,8] have shown an increase in postoperative complications at 30 days. In our series 13% of the operations were performed on diabetics, which is lower than the 39% reported by Akbari *et al.*[14] This raises the question whether they had an unusually high frequency of diabetes in their series or if there was a suboptimal identification of diabetes in our series? When compared to other large prospective multicentre series, European Carotid Surgery Trialist's Collaborative Group[7] (9% diabetics) and North American Symptomatic Carotid Endarterectomy Trial Collaborators[8] (17% diabetics in the surgical group), the frequency of diabetes in our series seems reasonable. We therefore believe that all patients with clinically relevant diabetes have been identified in our series. There was also a high frequency of operations for asymptomatic stenosis reported by Akbari *et al.*[14] (45% diabetics, 43% non-diabetics) compared to our series (8.8% diabetics, 9.5% non-diabetics). Both these characteristics point to special selection which was not the case in our population-based series.

During recent years there has been an increased awareness to identify and modify preoperative risk factors, and an improvement in the postoperative care of patients undergoing CEA. These may be factors leading to the significant decrease of postoperative morbidity and mortality in non-diabetic patients operated on in 1992–96 compared to 1987–91. However, there was no decrease in morbidity and mortality between the two periods in diabetic patients. This calls for an even more meticulous patient selection, risk factor identification, and medical optimising of the diabetic population considered for CEA. In conclusion, diabetics had a significantly higher 30-day and 1-year mortality, but they did not have a higher postoperative neurologic morbidity. The mortality was mainly cardiac. There was a significant decrease in postoperative morbidity and mortality in non-diabetics when operations early in the series were compared with more recent operations. This trend was not seen in the diabetics.

Acknowledgements

The present study was supported by the Swedish Medical Research Council grants no. 00759. Advice and help with statistical analysis by Stefan Sörensen, Department of Research, Västerås County Hospital. The centres and surgeons contributing to the Swedish Vascular Registry are listed below:

Centre	Surgeon
Borås	Christer Drott
Eskilstuna	Ingvar Jansson
Falun	Claes-Göran Björck
Göteborg	Jan Holm
Helsingborg	Gunnar Plate
Jönköping	Erik Svartholm

Kalmar	Antoni Potemkowski
Karlskrona	Bengt Jernby
Kristianstad	Mogens Thomsen
Linköping	Tommy Skau
Lund, *Department of Surgery*	Johan Thörne
Lund, *Department of Neurosurgery*	Wilhelm Schalén
Malmö	Thomas Mätzsch
Norrköping	Fredrik Lundgren
Stockholm-Huddinge	Björn Wiklund
Stockholm-KS	Linus Blohmé
Stockholm-SöS	Peter Konrad
Umeå	Conny Arnerlöv
Uppsala	Karl Logason
Västerås	Claes Forssell
Örebro	Björn Stenberg

References

1 Stegmayr B, Asplund K. Diabetes as a risk factor for stroke. A population perspective. *Diabetologia* 1995; **38**: 1061–1068.
2 Biller J, Love BB. Diabetes and stroke. *Med Clin North Am* 1993; **77**: 95–110.
3 Barret-Conner E, Khaw KT. Diabetes mellitus: an independent risk factor for stroke? *Am J Epidemiol* 1988; **128**: 116–123.
4 Tuomilehto J, Rastenyte D, Jousilahti P, Sarti C, Vartiainen E. Diabetes mellitus as a risk factor for death from stroke. Prospective study of the middle-aged Finnish population. *Stroke* 1996; **27**: 210–215.
5 Mankovsky BN, Metzger BE, Molitch ME, Biller J. Cerebrovascular disorders in patients with diabetes mellitus. *J Diabetes Complications* 1996; **10**: 228–242.
6 Chukwuma C Sr, Tuomilehto J. Diabetes and the risk of stroke. *J Diabetes Complications* 1993; **7**: 250–262.
7 European Carotid Surgery Trialists' Collaborative Group. MRC European Carotid Trial: interim results for symptomatic patients with severe (70–99%) or with mild (0–29%) carotid stenosis. *Lancet* 1991; **337**: 1235–1243.
8 North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade stenosis. *N Engl J Med* 1991; **325**: 445–453.
9 Mayberg MR, Wilson SE, Yatsu F *et al.* Carotid endarterectomy and prevention of cerebral ischemia in symptomatic carotid stenosis. *JAMA* 1991; **266**: 3289–3294.
10 L'Italien GJ, Cambria RP, Cutler BS *et al.* Comparative early and late cardiac morbidity among patients requiring different vascular surgery procedures. *J Vasc Surg* 1995; **21**: 935–944.
11 Mackey WC, O'Donnell TF Jr, Callow AD. Cardiac risk in patients undergoing carotid endarterectomy: impact on perioperative and long-term mortality. *J Vasc Surg* 1990; **11**: 226–234.
12 Salenius JP, Harju E, Riekkinen H. Early cerebral complications in carotid endarterectomy: risk factors. *J Cardiovasc Surg (Torino)* 1990; **31**: 162–167.
13 Skydell JL, Machleder HI, Baker JD, Busuttil RW, Moore WS. Incidence and mechanism of post-carotid endarterectomy hypertension. *Arch Surg* 1987; **122**: 1153–1155.
14 Akbari CM, Pomposelli FB Jr, Gibbons GW *et al.* Diabetes mellitus: A risk factor for carotid endarterectomy? *J Vasc Surg* 1997; **25**: 1070–1076.
15 Plecha EJ, King TA, Pitluk HC, Rubin JR. Risk assessment in patients undergoing carotid endarterectomy. *Cardiovasc Surg* 1993; **1**: 30–32.
16 Vascular Registry in Southern Sweden. Vascular registry in Southern Sweden – the first year experience of a Vascular Registry. *Eur J Vasc Surg* 1989; **3**: 563–569.
17 Bergqvist D, Einarsson E, Elfström J, Norgren L, Troëng T. Experience with the Swedish vascular registry. *Vasc Med Rev* 1994; **5**: 151–160.
18 Bergqvist D, Einarsson E, Elfström J, Norgren L, Troëng T. Vascular surgical audit during a 5-year period. *Eur J Vasc Surg* 1994; **8**: 472–477.
19 Rothwell P, Warlow C. Is self-audit reliable? *Lancet* 1995; **346**: 1623.
20 Moore WS, Barnett HJ, Beebe HG, Bernstein EF, Brener BI. Guidelines for carotid endarterectomy: a multidisciplinary consensus statement from the ad hoc committee, American Heart Association. *Stroke* 1995; **26**: 188–201.
21 Troëng T, Bergqvist D, Norrving B, Ahari A. Complications after carotid endarterectomy are related to surgical errors in less than one fifth of cases. *Eur J Vasc Endovasc Surg* (In press).

Accepted 22 January 1999